

Relapse of Herpes Simplex Encephalomyelitis Presenting As Guillain Barre Syndrome

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Abstract: Herpes simplex virus (HSV) is a well known etiological agent, rarely has been observed as a causative agent for Guillain Barre Syndrome. HSV has been associated with various neurological disorders like encephalitis & aseptic meningitis. Finger countable cases are reported of HSV associated with acute polyradiculopathy / GB Syndrome in the world literature^{1,2,3}. We have an opportunity of observing a fatal case of acute polyradiculopathy developed after short recovery with Acyclovir.

I. Case Report

A 70 year old male patient hospitalized in third week of September 2015, with complaints of severe headache, vomiting, fever, confusion, altered mental status and weakness in both lower limbs since past 4 days. He denied history of past seizure, tuberculosis, ischemic heart disease, leptic infections & previous viral infection such as Herpes Zoster or Herpes Labialis. Patient was hypertensive and diabetic past 06 yrs, well under control with medications. His vitals were normal, CNS examination revealed patient confused, disoriented and with weakness in both lower extremities. The superficial reflexes were normal and biceps, triceps jerks were normal, knee and ankle jerks were Brisk 4/5, plantar reflex were flexor bilaterally. Pupils were normal and reacting to light. Fundus examination was normal. The systemic examination was unrevealing. The clinical diagnosis of viral encephalomyelitis was entertained. Hematological and biochemical investigations done were unremarkable, X-ray chest was normal, lumbar puncture consent was not available. Serum samples were sent for HSV type 1 and 2 specific antibodies. Patient was put on IV Acyclovir 15mg/kg/day in divided doses 8hrly along with supportive therapies. The treatment was provided on clinical assumption of herpes simplex encephalomyelitis. Symptomatic improvement was observed within 48 hrs post antiviral therapy with recedence of clinical features. Serology of herpes simplex virus was reported positive for IgG - 26.2 (reference value >1.10 is considered positive). The positive – IgG antibody to HSV type 1&2 glycoprotein G detected indicate a current or past HSV infection. The antiviral doses were considered for the patient for maximum of 14 days. Patient condition improved significantly with subjective and objective vital parameters, with 14 days of anti viral and supportive therapies. On recovery the power in lower extremities was 5/5. Following discharge after 15 days, he remained mostly asymptomatic for next two weeks. Patient visited another hospital; the records revealed patient was having difficulty in walking and swallowing past 3days. He was afebrile, fully conscious, oriented with no signs of raised ICT or meningeal irritation. Flexors of the neck were weak with decreased Gag reflex, bilateral mild facial weakness noted. Power bilateral upper limbs were grade 3/5 and lower limbs grade 1/5, DTR in upper limbs was normal and lower limbs was absent. Plantar was flexors bilaterally, sensory examination done was grossly normal. Nerve conduction study with Electromyography carried out revealed symmetrical motor distal & proximal lower limb and upper limbs demyelinating axonal and peripheral neuropathy like GBS. Lumbar puncture done revealed proteins-85mg/dl, sugar-62mg/dl, chloride-136mg/dl, TLC- 4 cells/cumm, all were lymphocytes, simultaneous BSL-124mg/dl, ADA- 5.6 u/l. As patient developed difficulty in swallowing and breathing, was put on ventilatory support and central line infusion. With diagnosis of GBS, a course of IV immunoglobulin therapy was provided with palliative therapy. Patient's condition however, grew worse. He developed hypotension, Tachycardia, oliguria and rising creatinine values. He was planned for Dialysis and on patient request case was transferred to our hospital for further management. On reviewing documents and clinical examination, diagnosis of relapse of HSE presenting with GBS was entertained. Recourse of antiviral (Acyclovir) was started. His condition grew worse. Patient had further fall of blood pressure with 40 systolic, heart rate 120 per minute and respiratory embarrassment. Iontrophs and ventilator assistance were provided. Patient condition did not improve despite resuscitations and he succumbed to death 8 hrs after the present, second hospitalization. Post mortem was denied.

II. Discussion

Guillain Barre syndrome- acute inflammatory demyelinating disease is a relatively common neurological disorder but in situation with Herpes simplex infection co-existence remains an uncommon presentation. GB Syndrome has been observed to follow a variety of viral infections. Herpes simplex virus

association with GBS patient is only 1% ,as against other viral infection particularly those caused by Herpes viruses are Ebstein Barr Virus 10% , Cytomegalovirus 13% , Varicella Zoster 1% & other more recently described Human Herpes viruses HHV 6,7&8. ^{4,5}. The pathological features of GBS is multifocal noninfectious inflammatory process affecting peripheral nervous system, incorporating genetic environmental and immunological factors.⁶ Incidence of relapse of HSE is variably described as 5% to 25% even after acyclovir therapy.⁷ About 90% of persons are seropositive for HSV 1 suggesting past exposure to the virus, finding consistent with presence of latent HSV 1 genomes in trigeminal ganglion of pupil at unselected necropsy to extent of 85-90%.⁸ The latent HSV 1 may periodically be reactivated either spontaneously or following various triggers such as immune suppression , trauma, irradiations etc. Patient under discussion had diabetes mellitus past 06 yrs. HSV in association with GBS have been described in past however, the information available on subject is scanty.^{1,2} Most patients described by authors had complaints of cases referable to viral infection ranging from one month to several weeks. The case under discussion had no evidence of preceding viral infections before the onset of Herpes simplex encephalomyelitis and subsequent GBS development. Our patient appeared to have had motor disturbances. The diagnosis of Guillain Barre polyradiculopathy is based on the progressive symmetrical motor disturbances, the characteristic CSF finding of Albumino-Cytological dissociation , the nerve conduction velocity and EMG revealing Demyelinating Axonal and peripheral neuropathy in proximal lower and upper limbs of GBS type. The possibility of relapse HSV infection as a contributing cause of polyradiculopathy is strongly considered in the case. We find it most likely in our case HSV infection developing as reinfection rather than neo infection. The strongest argument for this being the great rise in HSV serum titre by CLIA for IgG = 26.2 (normal positive level interval > 1.1) & IgM negativity.

The positive IgG antibody to HSV type 1&2 glycoprotein G-specific antibody so detected may indicate a current or past HSV infection.⁹

Herpes simplex Virus type 1 & 2 are members of Herpes Viridae family and produce infections that may range from mild stomatitis to disseminated disease with fatal outcome. The clinical conditions associated are gingivostomatitis, keratitis, encephalitis, aseptic meningitis, genital infections and disseminated primary infection. HSV infections type 1 & 2 differ in their clinical presentations. Type 1 is closely associated with orolabial infection, genital infections in certain population. Type 2 primary infections are urogenital infections and most commonly and almost exclusively in adult. The routine diagnosis of disease is clinical one supported by laboratory testing (PCR or Viral culture) besides serological testing for IgG class antibodies to type specific HSV glycoprotein G-specific antibody. The test may be useful for either subclinical or unrecognized infection.

IgM antibody to HSV type 1 & or 2 by IgM ELISA may indicate current or recent infection however, low levels of IgM antibodies may occasionally persist for more than one month.

The present case had remarkable improvement within 24 to 36 hrs with IV acyclovir 500mg 8hry, therapy extended to 14 days. The patient had total recovery and discharged walking with normal vitals. He had second hospitalization after two weeks to another hospital with history of progressive weakness in bilateral lower limb and difficulty in swallowing and respiratory discomfort past 4 days. He was admitted in ICU where intubated, ventilated with central line done. A course of IV immunoglobulin therapy and supportive treatments were provided. Sooner he developed hypotension, tachycardia, acute renal failure and was planned for dialysis in leaf of rising creatinine values and oliguria. He was transferred to this hospital for further management. On reviewing documents and clinical examination diagnosis of relapse of HSE presenting with GBS was entertained. Recourse of antiviral (Acyclovir) was started. His condition grew worse in next couple of hours despite resuscitative measures adopted he succumbed to death 8 hrs after the present, second hospitalization. Consent for Post mortem was denied.

III. Conclusion

Herpes simplex virus (HSV) an etiological agent of various neurological disorders is rarely associated with radicular disorders of nervous system. We have been able to record one verified case of Guillain Barre Syndrome wherein HSV infection perhaps coexisted as reinfection rather than coexistent as neo infection.

Relapse of HSE can occur even in adequately treated case. Underlying immunoinflammatory and viral replication leading to relapse may bear an immense clinical significance as immunosuppressive therapy with steroids / intravenous immunoglobulin's / plasmapheresis may be required in selected cases depending on pathogenesis.

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